Sleep Medicine Reviews xxx (2014) 1–14

Contents lists available at ScienceDirect

Sleep Medicine Reviews

journal homepage: www.elsevier.com/locate/smrv

CLINICAL REVIEW

# Sleep disturbances of adult women suffering from fibromyalgia: A systematic review of observational studies

Carolina Diaz-Piedra [a, c, *], Leandro L. Di Stasi [a, b], Carol M. Baldwin [c], Gualberto Buela-Casal [a], Andres Catena [a]

[a] Mind, Brain, and Behavior Research Center-CIMCYC, University of Granada, Spain
[b] Department of Neurobiology, Barrow Neurological Institute, Phoenix, AZ, USA
[c] College of Nursing and Health Innovation, Arizona State University, Phoenix, AZ, USA

ARTICLE INFO

*Article history:*
Received 26 May 2014
Received in revised form
10 September 2014
Accepted 12 September 2014
Available online xxx

*Keywords:*
Actigraphy
Alpha-EEG sleep
Arousal
Chronic pain
Fibromyalgia
Polysomnography
Sleep

SUMMARY

Although sleep complaints are often reported in patients with fibromyalgia syndrome (FMS), there is no conclusive evidence that these complaints represent symptomatic disorders of sleep physiology. Thus, the question of the role of sleep disturbances as an etiological or maintenance factor in FMS remains open. This study identifies the subjective and objective characteristics of sleep disturbances in adult women diagnosed with FMS. We carried out a systematic review of publications since 1990, the publication year of the American College of Rheumatology criteria of FMS. We selected empirical studies comparing sleep characteristics of adult women with FMS and healthy women or women with rheumatic diseases. We identified 42 articles. Patients with FMS were more likely to exhibit sleep complaints and also a less efficient, lighter and fragmented sleep. The evidence of a FMS signature on objective measures of sleep is inconsistent, however, as the majority of studies lacks statistical power. Current evidence cannot confirm the role played by sleep physiology in the pathogenesis or maintenance of FMS symptoms; nonetheless, it is clear that sleep disturbances are present in this syndrome.



## Introduction

Fibromyalgia syndrome (FMS) is characterized by chronic widespread musculoskeletal pain and multiple tender points [1,2]. The prevalence rate of FMS in the general population is high, ranging from 1.3% to 4.7%, and is more common among middle-aged and older women [3]. The syndrome has a severe impact on health systems due to the frequent health care utilization and treatment costs [4]. Recent estimates suggest that, only in the United States, the costs for managing care of patients with FMS have a combined value of up to $10,000 per patient per year [5]. FMS also has a great impact on patients' and their relatives' quality of life as it is a significant source of suffering [6].

The new American College of Rheumatology (ACR) criteria for FMS [2] recognize the role of other non-specific pain-related symptoms in the severity of FMS. Thus, beyond pain, the diagnosis for FMS is now based on a large number of symptoms and comorbidities [2], including sleep disturbances, fatigue, headache and migraine syndrome, neuropathic disorders, anxiety and/or depression disorders [4,7]. Among these, sleep disturbance is one of the most common and relevant symptoms in FMS [8]. Experimental and clinical studies on the complex relationship between sleep and pain have shown that pain can disrupt sleep and, at the same time, sleep deprivation can enhance pain sensitivity [9]. This so-called *vicious cycle* clearly explains this incapacitating condition: a day with intense pain is followed by a night of poor sleep quality and a poor night's sleep is followed by a reduction of pain perception threshold – i.e., an increase in pain intensity [10]. Moreover, a recent review of longitudinal studies suggests that sleep disturbances portend future pain better than pain portends future sleep disturbances [11]. It is also known that other symptoms of FMS (e.g., psychological distress, fatigue) are intrinsically related to sleep disturbances [12]. Thus, the early recognition and management of sleep disturbances in FMS patients might help to ameliorate morbidity in this syndrome [13], as suggested by several clinical trials using cognitive-behavioral therapy for insomnia [14,15]. Additionally, the study of sleep physiology and sleep behavior in these specific patients might improve the explanatory power of

* Corresponding author. Dr. C. Diaz-Piedra; University of Granada, Mind, Brain, and Behavior Research Center-CIMCYC, Campus de Cartuja s/n, 18071 Granada, Spain. Tel.: +34 958245168; fax: +34 958243749.
*E-mail address:* dipie@ugr.es (C. Diaz-Piedra).

http://dx.doi.org/10.1016/j.smrv.2014.09.001
1087-0792/

**List of abbreviations**

| | |
|---|---|
| ACR | American College of Rheumatology |
| AKT | actigraphy |
| EEG | electroencephalography |
| EPHPP | effective public health practice project |
| FMS | fibromyalgia syndrome |
| NREM | non-REM sleep |
| PICOS | participants, interventions; comparisons, outcomes, study design |
| PSG | polysomnography |
| PSQI | Pittsburgh sleep quality index |
| REM | rapid eye movement |
| SWS | slow wave sleep |
| VAS | visual analogue scale |

models that try to relate the etiology of FMS to sleep disturbance [16–19].

*The present review*

Although subjective poor sleep quality is a consistent and relevant finding among patients with FMS [20], the presence of specific polysomnographic sleep patterns in FMS is not yet clear. In fact, more than two decades of sleep research in FMS have not yielded robust findings about a FMS signature on objective assessments of sleep parameters. Polysomnography (PSG), as the *gold* standard sleep measure, still has not revealed a unique and consistent FMS pattern in sleep architecture among patients. The conflicting findings across studies make integrative conclusions on the basis of PSG difficult. Several studies have found low sleep efficiency [21–23], long wake time after sleep onset [21,24,25], and high percentage of light sleep [21,23,26,27] to be common in FMS sleep patterns. Furthermore, some studies have suggested microstructure abnormalities in FMS patients, mainly an electroencephalography (EEG) non-REM sleep anomaly [19] characterized by high alpha frequency band power (7.5–11 Hz) (α-EEG sleep) [28]. Contrarily, several studies have reported minimal differences [25,29,30] or no abnormalities at all between FMS patients and controls [31], suggesting that sleep complaints in FMS only reflect sleep misperception (e.g., [32]). These discrepancies in results might be due to the heterogeneity that characterizes the clinical profiles of FMS patients [33] and to inconsistencies in the studies' methods and recording tools [9]. Thus, a systematic review of the methodology and overall quality of sleep studies in FMS, which has not been performed as of yet, could reconcile the contradictory results of these studies. Here, we reviewed observational studies that assessed objective and/or subjective sleep parameters in FMS patients compared with healthy controls and/or rheumatologic patients (sleep disturbances might be associated to various rheumatologic disorders, and not only to FMS [34]).

## Methods

*Study eligibility criteria*

We followed specific inclusion criteria to select the articles analyzed in this review following the "PICOS" approach [35] (see Table 1): 1) participants: adult women diagnosed with FMS according the ACR 1990 classification criteria [1]; 2) study design: observational designs (*ex post facto* studies); 3) comparisons: healthy women or women patients with other chronic rheumatic diseases; 4) reported outcomes: subjective and objective sleep parameters.

*Search methods*

We conducted a comprehensive search of the relevant peer reviewed articles by using four electronic bibliographic databases: SCOPUS, PsycINFO, Medline, and Lilacs/Ibecs. We included English and non-English (Spanish, Portuguese, and Italian) scientific literature published between 1990, the year that the ACR criteria for the classification of FMS was published [1], to May 15th, 2014. Search terms were: "fibromyalgia", "sleep*", "polysomnography", "PSG", "actigraphy", "AKT". The complete search algorithm with the keywords for each database is available upon request from the authors. To identify additional studies not found in the electronic search we also conducted a manual search of the bibliographies of each retrieved article. Additionally, we examined relevant grey literature (doctoral theses and reports) by using two online databases: OpenGrey and OAIster.

*Data collection and analysis*

*Selection of studies*

Initially, two independent reviewers screened titles and abstracts of the retrieved articles for relevance. Articles included by either reviewer were considered potentially relevant and eligible for full text screening. A discussion about the inclusion criteria for each article followed. This process continued until both reviewers reached a consensus. Finally, a third sleep researcher examined all the articles included from each database to ensure that the selected works fulfilled the study and report eligibility criteria. For those citations fulfilling the inclusion criteria, or for which inclusion or exclusion could not be ascertained, two researchers independently reviewed the full texts. Fig. 1 shows the detailed outline of the study selection process.

*Data extraction and management*

We assessed the selected articles using a standardized form, which included data regarding authors, date of publication, objective(s), research design, participants, instruments, outcomes, and results. The document with data extraction results is available upon request from the authors.

Outcomes of interest are described in Table 2. Subjective and objective sleep measures were reported as means and standard deviations. Effect sizes (Cohen's $d$) were calculated for each difference. If, in a given study, the information was not provided for an outcome, when possible we calculated the expected outcomes (i.e., combining means and standard deviations when outcomes were reported separated). Post-hoc power analyses were performed for each test using G*Power 3.1.3 (available at http://www.gpower.hhu.de/). Sample sizes for each group, computed effect sizes, and $\alpha = .05$ were introduced to obtain the power to detect a difference between means in outcomes of interest.

*Quality assessment and strength of evidence*

We assessed the methodological quality of the studies by using an adaptation of the Effective Public Health Practice Project's (EPHPP) tool [36]. This tool includes the following items: selection of participants and allocation bias, blinding, confounders, data collection methods, withdrawals and dropouts. The adaptations consisted of minor changes in several item descriptions regarding the *confounders* (ethnic group, sex, marital status/family, age, socioeconomic status, education, health status, medication intake, body mass index, physical activity levels, menopausal status) so

Please cite this article in press as: Diaz-Piedra C, et al., Sleep disturbances of adult women suffering from fibromyalgia: A systematic review of observational studies, Sleep Medicine Reviews (2014), http://dx.doi.org/10.1016/j.smrv.2014.09.001

**Table 1**
Summary of criteria for selecting studies and their rationale following the Cochrane PICOS approach.

| Study characteristics | | Rationale |
|---|---|---|
| P | **Types of participants** | |
| | Fibromyalgia patients | ACR criteria [1] are the most widely accepted and, for its value, have enhanced much of the research in the field of FMS. |
| | Diagnosed following the ACR 1990 classification criteria [1] | |
| | Adults (>18 y) | Adult FMS differs from juvenile FMS in diagnostic criteria and epidemiology [84]. |
| | Women | Pain sensitivity and response to analgesic drugs differ between sexes [85]. |
| I | **Types of interventions** | |
| | Not applicable. | Not applicable. |
| C | **Types of comparisons** | |
| | Healthy women or women patients diagnosed with any chronic rheumatoid disease, other than FMS. | Asymptomatic controls: population group without pain or sleep complaints. Rheumatoid disease patients: population group with pain and/or sleep complaints. |
| O | **Types of outcome measures** | |
| | Primary outcomes | Both subjective and objective sleep measures assess different aspects of an individual's sleep experience [86]. Therefore, all sleep variables are of interest to understand sleep disturbances among FMS patients. |
| | Subjective assessments related to sleep variables | |
| | Polysomnographic parameters | |
| | Actigraphic parameters | |
| S | **Types of studies** | |
| | Ex post facto studies | Comparative studies (i.e., case-control studies) examining sleep outcomes in at least two population groups (FMS vs. asymptomatic controls; FMS vs. rheumatoid disease patients). |

| Report characteristics | Rationale |
|---|---|
| **Years considered**: 1990–2014 | 1990 is the year that the ACR fibromyalgia classification criteria was published [1] |
| **Language**: English, Spanish, Portuguese, and Italian | To get an extensive search limiting language restrictions |
| **Publication status**: peer reviewed articles, doctoral theses, and reports | To get an extensive search including published and unpublished material from multiple sources |

*Note*. ACR = American College of Rheumatology; FMS = Fibromyalgia syndrome; PICOS = participants, interventions, comparisons, outcomes, study design.

that we could assess observational studies. Here, the assessment of the item *data collection methods* was only applied to sleep measurements. Each item was rated as strong, moderate, or weak, depending on the reported characteristics of each study. A global rating for each study was obtained. The "*quality assessment tool for included studies*" document is available upon request from the authors.

## Results

From a total of 1644 retrieved articles, 152 titles and abstracts were identified as potentially relevant. After excluding duplicate records and screening the full text, 44 articles fulfilled the inclusion criteria. Two of the articles were duplicate reports, since they were translations from Portuguese [37,38] to English [26,39] (in what follows, we will reference the English ones). It should be noted that a single study can be reported in several supplementary articles. This condition will be appropriately indicated within the review. Thus, we reviewed 34 studies that were reported in 42 articles.

### *Quality assessment and strength of evidence*

Following the EPHPP tool, we categorized the majority of included studies (84.2%) as "weak", and 6 studies (15.8%) as "moderate". This rating reflects a lack of methodological information provided, rather than evidence that indicated methodological weakness. When provided, weakness derived from the inadequate

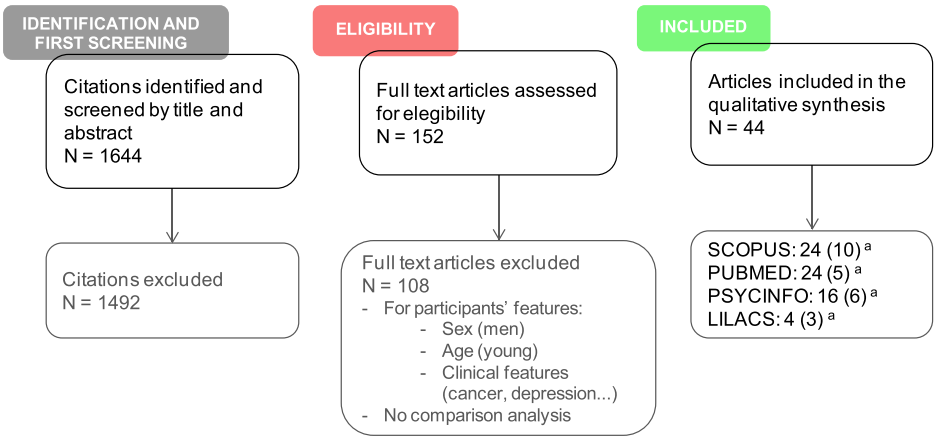


**Fig. 1.** Systematic review selection process. [a] Numbers in brackets are number of articles that appear only in the respective database.

Please cite this article in press as: Diaz-Piedra C, et al., Sleep disturbances of adult women suffering from fibromyalgia: A systematic review of observational studies, Sleep Medicine Reviews (2014), http://dx.doi.org/10.1016/j.smrv.2014.09.001

**Table 2**
Description of sleep outcome measures of interest.

| | |
|---|---|
| **Subjective measures** | |
| Sleep quality | Feelings about sleep duration, sleep latency, sleep depth, and restfulness |
| **Actigraphic parameters** | |
| Sleep efficiency | Percentage of total sleep time to time in bed |
| Nighttime activity levels | Counts of movements in each minute during time in bed |
| **Sleep architecture parameters** | |
| Time in bed (TIB) | Total amount of time between "lights out" and final awakening |
| Total sleep time (TST) | Total amount of sleep received from onset of sleep to onset of awakening |
| Sleep period time (SPT) | Period of time measured from sleep onset to final awakening |
| Sleep efficiency (SE) | Percentage of TST to TIB |
| Sleep latency N1 (SL N1) | Period of time between "lights out" and sleep onset (first epoch of stage 1, followed by six consecutive epochs of stage 1 or a deeper NREM sleep stage) |
| Sleep latency N2 (SL N2) | Peiod of time between "lights out" and the first epoch of stage 2 |
| Wake after sleep onset (WASO) | Period of wake time scored after sleep has been initiated and the final awakening |
| Wake percentage (W%) | Percentage of wake time scored from time in bed |
| Percentages of stage N1, stage N2, stage N3 (N1%, N2%, N3%) | Total time spent in stage 1, stage 2, and stage 3 NREM sleep as a percentage of TST, SPT, or TIB |
| Percentage of REM sleep (REM%) | Total time spent in REM sleep as a percentage of TST, SPT, or TIB |
| Sleep latency REM (SL REM) | Total amount of time between "lights out" and the first epoch of REM |
| Number of stage shifts | Number of sleep stage changes to wakefulness or another sleep stage |
| Number of awakenings | Number of epochs scored as wakefulness |
| Fragmentation index | Number of stage changes to wakefulness or stage N1 per hour |
| **Sleep microstructure parameters** | |
| Number of arousals | Abrupt change in the EEG activity consisting of $\alpha$ and $\theta$ waveforms (but not sleep spindles) and duration 3–15 s, preceded and followed by sleep |
| $\alpha$-EEG sleep | Power or percentage of the alpha frequency band (7.5–11 Hz) in NREM sleep |
| Spindles | Rapid EEG oscillations (10–16 Hz) lasting 0.5–2 s |

*Note*. EEG = Electroencephalography, REM = rapid eye movement.

**Table 3**
Summary of reviewed studies and quality assessment results from the Effective Public Health Practice Project's tool. Supplementary and duplicate reports are indicated in the first column.

| | Country | Sleep assessment | Effective Public Health Practice Project's tool | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | Selection bias | Study design | Confounders | Blinding | Data collection methods | Withdrawal/ drop-outs | Global rating |
| Akdoğan et al. 2013 [56] | Turkey | Subjective | M | M | W | M | ST | W | W |
| Akkaya et al. 2013 [48] | Turkey | Subjective | M | M | W | M | W | W | W |
| Bagge et al. 1998 [45] | Sweden | Subjective | W | M | W | M | W | W | W |
| Besteiro et al. 2011 [24] | Spain | PSG | M | M | W | M | ST | W | W |
| Borman & Çeliker 1999 [43] | Turkey | Subjective | W | M | W | M | ST | W | W |
| S Burns et al. 2008/Chervin et al. 2009 [29,30] | US | PSG | W | M | W | M | ST | W | W |
| Can & Can 2012 [57] | Turkey | Subjective | W | M | W | M | W | W | W |
| Côté & Moldofsky 1997 [67] | Canada | PSG | M | M | W | M | ST | W | W |
| Dick et al. 2008 [58] | Canada | Subjective | W | M | W | M | W | W | W |
| S Drewes et al. 1994, 1995a, 1995b [21,28,46] | Denmark | PSG | M | M | W | M | ST | W | W |
| Gur et al. 2002 [59] | Turkey | Subjective | W | M | W | M | W | W | W |
| Homann et al. 2013 [54] | Brazil | AKT/Subj | W | M | W | M | ST | M | W |
| Korszun et al. 2002 [13] | US | AKT/Subj | M | M | W | M | ST | W | W |
| Landis et al. 2003 [64] | US | AKT/Subj | M | M | M | M | ST | W | M |
| S Landis et al. 2004a [44] | US | PSG | M | M | M | M | ST | W | M |
| Landis et al. 2001 [22] | US | PSG | M | M | W | M | ST | W | W |
| Landis et al. 2004b [23] | US | PSG/Subj | M | M | M | M | ST | W | M |
| S Lario et al. 1996 [87] | Spain | PSG/Subj | M | M | W | M | ST | W | W |
| Lario et al. 1996 [88] | Spain | Subjective | M | M | W | M | W | W | W |
| Lerma et al. 2011 [49] | Mexico | Subjective | M | M | W | M | ST | W | W |
| Malin & Littlejohn 2012 [47] | Australia | Subjective | W | M | W | M | ST | W | W |
| D Martinez et al. 1994, 1995 [38,39] | Brazil | Subjective | W | M | W | M | ST | W | W |
| Martinez et al. 1998 [89] | Brazil | Subjective | M | M | W | M | ST | W | W |
| S Miró et al. 2012, 2011 [60,61] | Spain | Subjective | M | M | W | M | ST | W | W |
| Munguía & Legaz 2011 [50] | Spain | Subjective | W | M | M | M | ST | ST | M |
| Olama et al. 2013 [55] | Egypt | Subjective | M | M | M | M | W | W | W |
| Öncü et al. 2013 [90] | Turkey | Subjective | M | M | W | M | W | W | W |
| Osorio et al. 2006 [91] | Brazil | Subjective | M | M | W | M | ST | W | W |
| S Parrish et al. 2008/Zautra et al. 2007 [40,41] | US | Subjective | W | M | W | M | ST | ST | M |
| Riva et al. 2010 [66] | Norway | Subj/PSG | W | M | W | M | ST | W | W |
| Roehrs et al. 2013 [25] | US | PSG/Subj | M | M | W | M | ST | W | W |
| D Roizenblatt et al. 2001, 2002 [26,37] | Brazil | PSG/Subj | M | M | M | M | ST | W | M |
| Shaver et al. 1997 [27] | US | PSG/Subj | W | M | W | M | ST | W | W |
| Shaver et al. 2006 [42] | US | Subjective | W | M | W | M | W | W | W |
| Tander et al. 2007 [51] | Turkey | Subjective | W | M | M | M | W | W | W |
| Tüzün et al. 2004 [52] | Turkey | Subjective | M | M | W | M | W | W | W |
| Ulus et al. 2011 [53] | Turkey | Subjective | M | M | W | M | ST | W | W |

*Note*. AKT = Actigraphy; D = Duplicate reports; M = Moderate; PSG = Polysomnography; S = Supplementary reports; ST = Strong; Subj = Subjective assessment tool; W = Weak.

Please cite this article in press as: Diaz-Piedra C, et al., Sleep disturbances of adult women suffering from fibromyalgia: A systematic review of observational studies, Sleep Medicine Reviews (2014), http://dx.doi.org/10.1016/j.smrv.2014.09.001

control of confounders and insufficient information regarding withdrawals and drop-outs, as well as blinding of assessors and participants. Among studies using objective sleep assessment tools (PSG and actigraphy), four were categorized as moderate quality, whereas the remaining eleven studies showed weak quality. Two studies which carried out only a subjective assessment of sleep were categorized as moderate quality. The quality assessment results for included studies can be found in Table 3.

### *Characteristics of included studies*

#### *Study designs*

All studies were case-control studies, carried out in worldwide institutions. Turkish institutions were involved in the majority of the studies (9 studies). Studies were also conducted in the US (8 studies), Spain (4 studies), Brazil (5 studies), Denmark (1 study), Canada (2 studies), and Sweden, Norway, Mexico, Egypt, and Australia (1 study each).

#### *Participants*

Overall all 34 studies involved 3411 participants (1794 FMS patients, 1124 healthy controls, and 493 rheumatologic patients). In PSG studies, the average sample sizes were 24.0[10–40] FMS patients vs. 22.1[9–43] healthy controls. In questionnaire studies, the average sample sizes were 51.9[10–442] FMS patients vs. 31.7 [10–205] healthy controls. When comparisons were rheumatologic patients – one polysomnographic and ten subjective studies –, mean study sizes were 41.3[18–90] FMS patients vs. 44.8[16–89] rheumatologic patients.

The majority of samples were matched for age (89.5% of studies, except two studies that found age differences between groups [40–42] and two that did not contain age information [13,43]). One article used the variable age as covariate as well (i.e., [44]). Health status was controlled in the majority of studies (84.2%) (this information was not available for [13,21,28,38,43,45–47]). Several studies have matched their samples for body mass index (42.1%) [22,23,26,27,29,30,44,45,48–55], and/or educational level (42.1%) [24,26,27,40,41,48,50–53,55–61]. The majority of studies (71.1%) did not report participants' menopausal status. When menopausal status was reported, six studies selected homogenous samples (premenopausal [47,49,54,56,59]; postmenopausal [26]), while the other articles used heterogeneous samples, with [22,42,44] or without [27,29,30,44] significant differences in this variable.

**Table 4**
Summary of sample's characteristics of reviewed studies, including the definition of the groups of participants, sample sizes, setting of care reported, and the method of recruitment.

| Authors, reference | N FMS | Setting | Method of recruitment | Comparison group | N comparison group | Setting | Method of recruitment |
|---|---|---|---|---|---|---|---|
| Akdoğan et al. [56] | 40 | N/A | N/A | HC/RA | 30/28 | N/A | N/A |
| Akkaya et al. [48] | 48 | PHC | Volunteers from medical records | HC | 32 | Staff's relatives | Volunteers |
| Bagge et al. [45] | 10 | N/A | N/A | HC | 10 | N/A | N/A |
| Besteiro et al. [24] | 32 | PHC | Selected consecutively | HC | 20 | Unclear | Volunteers |
| Borman & Çeliker [43] | 22 | N/A | N/A | HC | 25 | Staff | Volunteers |
| Burns et al./Chervin et al. [29,30] | 15 | PHC | From referrals/advertisements | HC | 15 | Com. | Volunteers |
| Can & Can [57] | 63 | N/A | N/A | HC | 62 | N/A | N/A |
| Côté & Moldofsky [67] | 10 | PHC | From referrals/patients' files | HC | 9 | Com. | Volunteers |
| Dick et al. [58] | 30 | PHC/Com. | Volunteers | HC | 30 | PHC/Com. | Volunteers |
| Drewes et al. [21,28,46] | 14 | PHC | Selected consecutively | HC | 12 | N/A | N/A |
| Gur et al. [59] | 19 | PHC | N/A | HC | 20 | Com. | Volunteers |
| Homann et al. [54] | 17 | PHC | Volunteers | HC | 16 | University employees | Volunteers |
| Korszun et al. [13] | 16 | PHC | Selected consecutively | HC | 28 | N/A | Volunteers |
| Landis et al. [64] | 23 | PHC | Volunteers from referrals | HC | 22 | Com. | Volunteers |
| Landis et al. [22] | 25 | PHC | Volunteers from referrals | HC | 21 | Com. | Volunteers |
| Landis et al. [44] | 37 | PHC | Volunteers from referrals | HC | 30 | Com. | Volunteers |
| Landis et al. [23] | 33 | PHC | Volunteers from referrals | HC | 37 | Com. | Volunteers |
| Lario et al. [87] | 28 | PHC | Selected consecutively | RP | 15 | N/A | N/A |
| Lario et al. [88] | 60 | PHC | Selected consecutively | RP | 60 | PHC | Selected consecutively |
| Lerma et al. [49] | 22 | PHC | From referrals | HC | 22 | Staff | Volunteers |
| Malin & Littlejohn [47] | 25 | PHC/ECF/Com. | Volunteers | HC | 27 | Com. | Volunteers |
| Martinez et al. [39] | 44 | PHC | Selected consecutively | RA | 41 | PHC | Selected consecutively |
| Martinez et al. [89] | 26 | PHC | Selected consecutively | MPS | 18 | PHC | Selected consecutively |
| Miró et al. [61] | 90 | PHC/ECF | From referrals | HC | 70 | Com. | Volunteers |
| Miró et al. [60] | 104 | PHC/ECF | From referrals | HC | 86 | Com. | Volunteers |
| Munguía & Legaz [50] | 66 | ECF | Volunteers | HC | 48 | N/A | N/A |
| Olama et al. [55] | 50 | PHC | Selected consecutively | HC | 50 | Hospital staff | N/A |
| Öncü et al. [90] | 45 | PHC | Selected consecutively | RA | 44 | PHC | Selected consecutively |
| Osorio et al. [91] | 30 | PHC | Selected consecutively | HC | 30 | Patients' companions | N/A |
| Parrish et al./Zautra et al. [40,41] | 90 | PHC/ECF/Com. | Volunteers | RA/OA | 89/76 | PHC/ECF/Com. | Volunteers |
| Riva et al. [66] | 29 | ECF | Volunteers | HC | 29 | Blood donors | Volunteers |
| Roehrs et al. [25] | 18 | PHC/Com. | From referrals/volunteers | HC/RA | 16/16 | Com. | Volunteers |
| Roizenblatt et al. [26] | 40 | PHC | Randomly selected from a list | HC | 43 | Com. | Volunteers |
| Shaver et al. [27] | 11 | Com. | Volunteers | HC | 11 | Com. | Volunteers |
| Shaver et al. [42] | 442 | PHC/ECF/Com. | Volunteers | HC | 205 | Patients' relatives/Com. | Volunteers |
| Tander et al. [51] | 47 | N/A | N/A | HC | 28 | N/A | N/A |
| Tüzün et al. [52] | 33 | PHC | Selected consecutively | RA/MPS | 33/33 | PHC | Selected consecutively |
| Ulus et al. [53] | 40 | PHC | N/A | HC/RA | 40/40 | PHC/N/A | N/A |

*Note*. Com. = Community; ECF = Extended care facility; FMS = Fibromyalgia syndrome; HC = Healthy controls; MPS = Myofascial pain syndrome; N/A = Without information or not applicable; OA = Osteoarthritis; PHC = Primary health center; RA = Rheumatoid arthritis; RP = Rheumatologic patients.

Please cite this article in press as: Diaz-Piedra C, et al., Sleep disturbances of adult women suffering from fibromyalgia: A systematic review of observational studies, Sleep Medicine Reviews (2014), http://dx.doi.org/10.1016/j.smrv.2014.09.001

*Comparisons*

The comparison groups generally were composed of healthy control women (31 studies), or patients suffering from rheumatoid arthritis (7 studies), osteoarthritis (1 study), or myofascial pain (2 studies). Some studies included a combination of three groups (generally, FMS, healthy controls, and a rheumatologic patients group). The sample's characteristics of reviewed studies are displayed in Table 4.

*Outcomes assessment*

For the assessment of sleep outcomes, PSG was used in 13 studies, and actigraphy was used in 3 studies. Self-reports were used in 29 studies. Eight studies used both objective and subjective sleep assessment tools.

*Subjective sleep assessment tools*

The methods to subjectively assess sleep outcomes (primarily sleep quality and daytime sleepiness) included questionnaires (validated sleep questionnaires were used in 13 studies out of 19 [sleep subscales from other questionnaires were used in 5 studies]), visual analogue scales (VAS, 4 studies), Likert-like scales (2 studies), and questions created *ad hoc* (4 studies) (see Table 5). None of those sleep measures has been validated in chronic pain populations. The most common tool used to assess sleep quality was the Pittsburgh sleep quality index (PSQI) that was used in 9 studies. The mean PSQI scores in women with FMS ranged from 5.20 to 15.15, consistently higher than the established cut-off to classify people as having sleep disturbances [62,63]. All studies using PSQI had a statistical power of 0.99–1.00 to detect differences between groups.

Regardless of the specific subjective sleep assessment tool, when compared to healthy controls women with FMS reported poorer sleep quality, fewer hours of sleep, greater nighttime awakenings, and non-restorative sleep. When compared to other clinical populations that included rheumatoid arthritis, osteoarthritis or myofascial pain, women with FMS reported poorer sleep quality (except one study that did not found differences [39]). Scores from sleep quality questionnaires are summarized in Table 6.

*Objective sleep assessment tools*

*Actigraphy (AKT).* Three studies used actigraphic assessment to study the characteristics of sleep disturbances in women with FMS [13,54,64]. The number of days assessed were 8 [54], 5–7 [13], and 3 d [64]. Wrist actigraphy was used and participants scored their activity data and sleep-wake times in written diaries. Two studies found that FMS patients outscored healthy controls in nighttime activity levels [13,54]. FMS patients showed less sleep efficiency than healthy controls in one study (see Table 7).

*Polysomnography (PSG).* Table 8 shows the main protocol characteristics used in the PSG studies reviewed. Specific details about the assessment of sleep microstructure are shown in Table 9. Nine out of ten polysomnographic studies used the Rechtschaffen and Kales scoring criteria [65]. All studies, except three [25,29,30], did not report the number of sleep scorers, their blinding conditions, and/or the established minimum level of agreement between

**Table 5**
Summary of subjective sleep assessment tools to assess sleep outcomes in the reviewed studies.

| Authors, reference | Subjective sleep assessment tools | Validation |
|---|---|---|
| Akdoğan et al. [56] | Pittsburgh sleep quality index | Yes |
| Akkaya et al. [48] | Pittsburgh sleep quality index | Not for this population |
| Bagge et al. [45] | VAS in mm (0–100): sleep quality during last month/last week | No |
| Borman & Çeliker [43] | Sleep subscale of the Nottingham health profile | Yes |
| Can & Can [57] | VAS in mm (0–100): sleep disturbances last week | No |
| Dick et al. [58] | Average total hours of sleep<br>Average number of awakenings per night<br>Time period not specified | No |
| Gur et al. [59] | Likert scale: sleep disturbances<br>Time period not specified | Not for this population |
| Homann et al. [54] | Sleep diary | No |
| Landis et al. [64] | Sleep items from the Washington women's health diary | Yes (whole diary), reliability assessed *ad hoc* |
| Landis et al. [23] | Likert scale: sleep quality, awaken feeling rested and alert | No |
| Lario et al. [87] | Epworth sleepiness scale | Not for this population |
| Lario et al. [88] | Campbell's questionnaire | Not for this population |
| Lerma et al. [49] | Medical outcome sleep scale | Yes (without reference) |
| Malin & Littlejohn [47] | Sleep subscale of the fibromyalgia impact questionnaire | Yes |
| Martinez et al. [39,89] | Modified post-sleep inventory | Not for this population |
| Miró et al. [60,61] | Pittsburgh sleep quality index | Yes |
| Munguía & Legaz [50] | Pittsburgh sleep quality index | Yes |
| Olama et al. [55] | Pittsburgh sleep quality index | No |
| Öncü et al. [90] | VAS in mm (0–100): average amount of sleep over the last week | No |
| Osorio et al. | Pittsburgh sleep quality index | Yes |
| Parrish et al./Zautra et al. [40,41] | Pittsburgh sleep quality index | Yes |
| Riva et al. [66] | One question (sleep problems) of the subjective health complaints inventory | Yes (whole inventory) |
| Roehrs et al. [25] | Epworth sleepiness scale | Yes |
| Roizenblatt et al. [26] | Questionário dos distúrbios do sono | Yes |
| Shaver et al. [27] | Items from the specific health symptom questionnaire | No, reliability assessed *ad hoc* |
| Shaver et al. [42] | Questions about sleep-related diagnoses and lifestyle behaviors related to sleep pattern | No |
| Tander et al. [51] | VAS in mm (0–100): sleep disturbance. Time period not specified | No |
| Tüzün et al. [52] | One question about sleep | No |
| Ulus et al. [53] | Pittsburgh sleep quality index | Yes |

*Note.* VAS = Visual analogue scale.

Please cite this article in press as: Diaz-Piedra C, et al., Sleep disturbances of adult women suffering from fibromyalgia: A systematic review of observational studies, Sleep Medicine Reviews (2014), http://dx.doi.org/10.1016/j.smrv.2014.09.001

**Table 6**
Comparison of sleep quality questionnaire scores in patients with fibromyalgia syndrome vs. healthy controls (6.a) and vs. rheumatologic patients (6.b).

| | FMS | HC | ES |
|---|---|---|---|
| | M(SD) | | *d* |
| *Pittsburgh sleep quality index-total* | | | |
| Akdoğan et al. [56] | 11 [1–20]*[a] | 0 [0–10] | *N/A* |
| Akkaya et al. [48] | 10.8 (4.4)* | 4.2 (3.2) | 1.715 |
| Miró et al. [60] | 15.1 (3.9)* | 5.0 (3.2) | 2.831 |
| Miró et al. [61] | 15.1 (4.0)* | 6.1 (3.4) | 2.424 |
| Munguía & Legaz [50] | 11.6 (3.7)* | 7.2 (4.8) | 1.026 |
| Olama et al. [55] | 5.2 (2.7)* | 2.3 (1.5) | 1.327 |
| Osorio et al. [91] | 12 [10–16]*[b] | 3 [2–5] | *N/A* |
| Ulus et al. [53] | 9.7 (4.3)* | 2.8 (2.1) | 2.039 |
| *Medical outcome sleep scale* | | | |
| Lerma et al. [49] | 60.5 (11.2)* | 19.2 (10.4) | 3.821 |
| *Questionário dos distúrbios do sono* | | | |
| Roizenblatt et al. [26] | 3.8 (2.0)*[c] | 8.4 (1.8) | −2.417 |
| | FMS | RA&OA | ES |
| | M(SD) | | *d* |
| *Pittsburgh sleep quality index-total* | | | |
| Akdoğan et al. [56] | 11 [1–20]*[a] | 4 [0–16] | *N/A* |
| Parrish et al./Zautra et al. [40,41] | 12.2 (3.5)* | 8.3 (4.0) | 1.035 |
| | FMS | MPS | ES |
| | M(SD) | | *d* |
| *Modified post-sleep inventory* | | | |
| Martinez et al. [39] | 64.6 (20.0) | 57.2 (21.3) | 0.163 |
| Martinez et al. [89] | 81.2 [29.0–100]*[a] | 64.6 [35–110] | *N/A* |

*Note*. ES = Effect size; FMS = Fibromyalgia syndrome; HC = Healthy controls; M = Mean; MPS = Myofascial pain syndrome; N/A = Not applicable; OA = Osteoarthritis; RA = Rheumatoid arthritis; SD = Standard deviation. A negative Cohen's *d* value represents that controls' scores are higher.
*$p < .05$.
[a] Results are expressed as median [minimum – maximum].
[b] Results are expressed as median [25–75%].
[c] Lower scores represent poorer sleep quality.

scorers. Most of the studies (60%) were conducted in a sleep laboratory during 2–3 nights. Only one study collected ambulatory data [21,28,46]. The time of PSG recording varied from laboratory fixed schedules (e.g., 8 h) to participants' usual schedules and a mixture of both options. The montage always included EEG channels (central derivations were used in all studies), bilateral electrooculography, and chin electromyography. The inclusion of other different PSG and electrocardiographic channels varied among studies.

Controls related to participants' physiological status at the time of the polysomnographic assessment are taken into account in almost all studies. Nearly all studies controlled for medication intake (80%) (which was suppressed from 2 d to 3 m prior assessment), or by recruiting patients who do not take medications. Most of the studies have controlled for the consumption of psychotropic substances prior to the PSG, including tobacco, alcohol, or caffeine (40%); however, few studies instructed participants to not take naps (10%) or have controlled menstrual cycle status in pre-menopausal women (10%).

From the ten PSG studies, nine reported PSG data (see Tables 10 and 11). The most common differences between FMS patients and healthy controls were found in sleep efficiency (4 studies [21–23,66], with an average statistical power of 0.46 ± 0.33), time of sleep spent in light sleep (non-REM N1 stage in 5 studies [21,23,26,27,67] and N2 stage in other 2 studies [23,24], with an average statistical power of 0.49 ± 0.32 and 0.45 ± 0.36, respectively) and time of wakefulness after sleep onset (3 studies [21,24,25], with an average statistical power of 0.67 ± 0.44). Only one study examined PSG in FMS and RA patients [25], revealing non-significant differences between groups on any PSG outcome.

Six studies examined differences in α-EEG sleep (without a consensus about its definition) between FMS patients and healthy controls. One study found differences in the α-power during non-REM sleep [21], which was greater in FMS patients, and another study observed an EEG pattern of low alpha [26] to be more common in healthy controls. Additionally, one study characterized sleep spindles in FMS, which were less frequent and with lower sigma power [44] than healthy controls.

## Discussion

In this systematic review, our aim was to identify the characteristics of sleep disturbances in adult women diagnosed with FMS. We found that women with FMS systematically reported more sleep symptoms (poorer sleep quality, more complaints of insufficient sleep, a great number of awakenings, and/or the experience of unrefreshing sleep) when compared to healthy controls (or other rheumatologic patients). Moreover, the effect sizes were in the "large" range (greater than 0.8 [68]), and these comparisons had sufficient power to detect a "large" size difference between patients and controls from questionnaire results ($1 - \beta = [0.99–1.00]$). Evidence from objective measures of sleep in patients with FMS was mixed and inconsistent, however. When compared with a healthy population (data from PSG studies involving other rheumatologic patients is exceptionally scarce), the most common findings among women with FMS were: higher proportion of light sleep (greater time spent in non-REM N1 stage [21,23,26,27,67] and N2 stage [23,24]), reduced sleep efficiency (corroborated by PSG [21–23,66] [24] and AKT [54] studies), and more fragmented sleep (greater time of wakefulness after sleep onset [21,24,25]). Furthermore, although studies did not uniformly report the same sleep outcomes, all studies found at least one difference in the categories of PSG parameters established by Shaver and colleagues [27] – overall

**Table 7**
Comparison of actigraphic parameters in patients with fibromyalgia syndrome vs. healthy controls.

| | Sleep efficiency (%) | | | Nighttime activity (/min) | | | Fragmentation index | | |
|---|---|---|---|---|---|---|---|---|---|
| | FMS | HC | ES | FMS | HC | ES | FMS | HC | ES |
| | M(SD) | | *d* | M(SD) | | *d* | M(SD) | | *d* |
| Homann et al. [54] | 81.5 (7.7)* | 86.5 (4.8) | −0.779 | 462.7 (237.9)*[a] | 300.1 (126.6) | 0.853 | *N/A* | | |
| Korszun et al. [13] | 92.2 (1.0) | 89.1 (1.8) | 2.089 | 19.5 (2.0)*[b] | 7.7 (1.2) | 7.154 | *N/A* | | |
| Landis et al. [64] | 81.7 (8.1) | 81.2 (10.4) | 0.053 | *N/A* | | | 3.2 (0.8) | 3.2 (0.7) | 0.000 |

*Note*. ES = Effect size; FMS = Fibromyalgia syndrome; HC = Healthy controls; M = Mean; N/A = Not measured; SD = Standard deviation. A negative Cohen's *d* value represents that controls' results are higher.
*$p < .05$.
[a] Presence of movement in each minute.
[b] Counts of activity level generated by the device during each minute.

Please cite this article in press as: Diaz-Piedra C, et al., Sleep disturbances of adult women suffering from fibromyalgia: A systematic review of observational studies, Sleep Medicine Reviews (2014), http://dx.doi.org/10.1016/j.smrv.2014.09.001

**Table 8**
Summary of protocol features of polysomnographic assessment (10 studies).

| Authors, reference | Scoring criteria | N sleep scorers/ agreement | Blinding | Automatic scoring | Setting | Time of recording | PSG equipment/montage | Physiological status controls |
|---|---|---|---|---|---|---|---|---|
| Besteiro et al. [24] | R&K | N/A | N/A | No | Sleep laboratory at hospital<br>1 night | 8 h<br>Fixed: 23:00–7:00 | 32-channel *Discovery* EEG (Medelec Vickers Medical, Inc.)<br>Cz/A1-O1/A1<br>EOG/EMG/EKG<br>Polygraphic channels | - Without medication that could affect sleep 3 m prior PSG |
| Burns et al./Chervin et al. [29,30] | R&K | 1[a]/N/A | Yes | No | Sleep laboratory at clinical research center<br>3 nights | N/A | Telefactor DEEG/TWIN F3/A2-F4/A1-C3/A2-C4/A1-O1/A2-O2/A1<br>EOG/EMG/EKG<br>Polygraphic channels | - Without psychotropic medications, hypnotics, analgesics, and herbal or over-the-counter supplements 2 wk prior PSG<br>- Without acetaminophen and diphenhydramine 3 d prior PSG<br>- Without caffeine, nicotine, or alcohol 3 d prior study |
| Côté & Moldofsky [67] | R&K | N/A (1, for alpha scoring) | N/A (Yes, for alpha scoring) | No | Sleep laboratory<br>2 nights | Fixed: 22:30–7:00 | Oxford Medilog 9000 recorder<br>C3/A2-C4/A1-O1/A2-O2/A1<br>EOG/EMG<br>Polygraphic channels | - Without medication<br>- Nonsmokers |
| Drewes et al. [21,28,46] | R&K | N/A | Yes | No | In-home<br>2 nights | 7.30 h<br>Participants' usual sleep schedule | Judex Datasystems A/S, Denmark<br>F3/A2-C4/A1<br>EOG/EMG<br>Polygraphic channels | - Without psychotropic medications 2 wk prior PSG<br>- Caffeine, nicotine, or alcohol allowed until 18:00 |
| Landis et al. [22,23,44] | R&K | 1<br>>90% agreement | N/A | Yes,<br>Oxford Sleep Acquisition Computer system | Sleep laboratory at research center<br>3 nights | Participants' usual bedtime – 07:00 | Grass model 7 polygraph<br>C3/A2-Fz/A1-A2-Cz/A1-A2<br>EOG/EMG<br>Polygraphic channels | - Without psychotropic, hypnotic, or sedative medications 2 wk prior PSG<br>- Caffeine, nicotine, or alcohol allowed until 13:00.<br>- Naps not allowed<br>- PSG 5–10 d following menses |
| Lario et al. [87] | R&K | N/A | N/A | N/A | Standard hospital room<br>N of nights not reported | N/A | N/A<br>F3/C3-F4/C4-C3/A2-C4/A1<br>EOG/EMG/EKG<br>Polygraphic channels | N/A |
| Riva et al. [66] | Iber et al. 2007 | N/A | N/A | N/A | Hospital hotel<br>1 night | Interval since 22:15–01:00 to 05:00–07:30 | N/A<br>2 EEG channels<br>EOG/EMG/EKG<br>Polygraphic channels | - Without medication that interact with neural, vascular, or muscular function or psychophysiological measures<br>- Without analgesics and/or sleep medicines 2 d prior PSG |
| Roehrs et al. [25] | R&K | 2<br>90% | Yes | No | Sleep laboratory at hospital<br>2 nights | 8 h<br>Participants' usual sleep schedule | N/A<br>C3/A2-O2/A1<br>EOG/EMG | - Without medication that could affect sleep, including antidepressants<br>- Without pain medications (NSAIDS, opioids, other analgesics) 1 wk prior PSG |
| Roizenblatt et al. [26] | R&K | N/A | Yes | No | Sleep laboratory<br>2 nights | N/A | 9.2 Medilog Sleep Analyzer Computer<br>C3/A2-C4/A1-Oz/Fz<br>EOG/EMG/EKG<br>Polygraphic channels | - Without medication that could affect sleep 1 m prior PSG.<br>- Without caffeine, nicotine, or alcohol 1 d prior study |
| Shaver et al. [27] | R&K | N/A<br>92% | Yes | Yes,<br>Oxford Sleep Acquisition Computer system | Sleep laboratory<br>2 nights | Typical hours for duration of sleep length | Oxford Sleep Acquisition Computer system<br>C3/A2-C4/A1<br>EOG/EMG<br>Polygraphic channels | - PSG 4–10 d following menses |

*Note*. EEG = Electroencephalography; EKG = Electrocardiography; EMG = Electromyography; EOG = Electrooculography; N = Number; N/A = Without information or not applicable; NSAIDS = Non-steroidal anti-inflammatory drugs; R&A = Rechtschaffen and Kales; PSG = Polysomnography.

[a] Borderline PSG features were discussed with an investigator.

sleep quality (including sleep efficiency and sleep latency [21,23]), sleep depth (including less time spent in N3 stage [24]), and sleep continuity (including sleep changes [30] and fragmentation index [22]) or arousal activity [24] – but the relevance of these measurements to explain sleep health is far from clear [69]. Additionally, effect sizes varied considerably among studies for the PSG outcomes, from "moderate" to "large" [68]. More importantly, the average statistical power of all hypothesis tests across all PSG studies ranged from 25% to 67%, far from the power found in subjective studies. For example, the power of studies to detect "moderate" to "large" size differences between groups in sleep efficiency, time of wakefulness after sleep onset and light sleep percentage ranged from 45 to 67%. The implication of this finding is that within PSG studies, a sizeable chance existed for researchers to erroneously conclude that PSG disturbances were absent among FMS patients.

Data from the included studies showed that the characterization of a FMS signature on objective patterns of sleep is still challenging. Discrepancies in PSG data might be due to methodological inconsistencies among studies, involving, for example, sample size, sample selection criteria, or different protocols of sleep assessment. Therefore, an assessment of study biases seems useful to fully understand the results of this review and their implications. The presence of basic methodological weaknesses among studies was frequent, and only three PSG studies have moderate quality [23,26,44] (according to the EPHPP criterion). Consequently, available data should be interpreted with caution. It has to be noted, however, that several studies were conducted before the publication of the guidelines to assess the quality of reports (or risk of bias) [73,74]. Future studies should attempt to overcome the methodological issues of studies identified in this review.

As commented before, relevant methodological concerns are sample size as well as both sociodemographic and clinical variables. Firstly, due to the small number of participants, many of the identified studies lack the power to reject a false null hypothesis. Indeed, five studies involved less than twenty participants per group, with scarce differences between patients and controls [25,27,29,30,67] (but see [21,28,46]). When more than forty participants per group were recruited, as was the case with subjective studies, statistical power increased to adequate levels (more than 0.95) [26] (these authors reported findings incompletely, however). Secondly, sociodemographic and clinical variables can account for differences in sleep behavior [70,71]. Age, gender, ethnic group, educational level, and marital status are important contributing factors to understand sleep health. Body mass index, menopausal status, physical activity levels, health status, and medications also alter sleep. For this reason, some studies have tried to match participants from clinical and control groups for several of these variables, mainly for age, gender, health status, education, and body mass index. Other relevant variables (especially ethnic group, socioeconomic status, menopausal status, and physiological status) have been neglected in several of the reviewed studies as well. In PSG studies of FMS, nuisance and uncontrolled variables are especially undesirable because PSG, as other biomedical signals, exhibits a low signal to noise ratio [72]. Regarding protocols of sleep assessment, although PSG devices were always digital, recording parameters varied across studies. Many of them did not follow the American Academy of Sleep Medicine guidelines (i.e., a minimum of three EEG derivations [frontal, central, and occipital] with a minimum sample rate of 200 Hz) [73]. Additionally, PSG is often considered as a non-ecological measurement because recordings have to be done in sleep laboratories. All studies except one [21,28,46] were conducted in PSG laboratories. Although researchers and sleep technicians take precautions to reduce discomfort in sleeping environments and, in particular, the *first night effect*, sleep laboratories are still artificial compared to home settings. In recent years, however, user-friendly commercial and portable PSG devices have overcome some drawbacks of classical PSG (i.e., technical and methodological difficulties of measuring these signals out of controlled settings, and the intrusiveness and bulkiness of the equipment).

Another explanation for the incongruences among PSG results comes from the intrinsic heterogeneity that characterizes the FMS

**Table 9**
Features of the sleep microstructure recording and analysis (7 studies).

| Authors, reference | N channels | Brain lobe analyzed | Reference electrodes | Filters | Sampling frequency | Artifact rejection | Signal segmentation | Signal analysis |
|---|---|---|---|---|---|---|---|---|
| Besteiro et al. [24] | N/A | N/A | Bipolar reference (A1) | N/A | N/A | N/A | N/A | Visual alpha scoring |
| Chervin et al. [30] | 1 | Central<br>Left hemisphere: C3 | Bipolar reference (A2) | N/A | 200 Hz | N/A | 1 s | Fourier power analysis |
| Côté & Moldofsky [67] | 4 | Central<br>Both hemispheres: C3/C4<br>Occipital<br>Both hemispheres: O1/O2 | Bipolar reference (A1/A2) | N/A | N/A | N/A | N/A | Visual alpha scoring |
| Drewes et al. [21,28,46] | 1 | Frontal<br>Left hemisphere: F1 | Bipolar reference (A2) | Highpass: 0.5 Hz<br>Lowpass: 25 Hz<br>Notch filter 50 Hz | 100 Hz | EEG samples without artifacts, but procedure is not explained | 2 s | Power spectral analysis by autoregressive modeling |
| Landis et al. [44] | 3 | Central<br>Left hemisphere and vertex: C3/Cz<br>Frontal<br>Midline: Fz | Bipolar reference (A2)<br>Linked-mastoids: A1-A2 | N/A | 250 Hz | Data with temporary spikes, sweating and/or body movements were removed | 2 s | Fourier power analysis |
| Roizenblatt et al. [26] | 2 | Central<br>Both hemispheres: C3/C4 | Bipolar reference (A1/A2) | Highpass: 0.3 Hz<br>Lowpass: 90 Hz | 500 Hz | | 2 s | Waveform analysis<br>Fourier power analysis<br>Visual alpha scoring |
| Shaver et al. [27] | 2 | Central<br>Both hemispheres: C3/C4 | Bipolar reference (A1/A2) | N/A | N/A | N/A | N/A | Visual alpha scoring |

*Note*. N = Number; N/A = Without information or not applicable.

Please cite this article in press as: Diaz-Piedra C, et al., Sleep disturbances of adult women suffering from fibromyalgia: A systematic review of observational studies, Sleep Medicine Reviews (2014), http://dx.doi.org/10.1016/j.smrv.2014.09.001

**Table 10**
Comparison of polysomnographic parameters in patients with fibromyalgia syndrome vs. healthy controls.

| | Time in bed (h) | | | Sleep period time (h) | | | Total sleep time (h) | | | Sleep efficiency (%) | | | WASO (min) | | | Wake (% SPT) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | FMS | HC | ES | FMS | HC | ES | FMS | HC | ES | FMS | HC | ES | FMS | HC | ES | FMS | HC | ES |
| | M (SD) | | *d* | M (SD) | | *d* | M (SD) | | *d* | M (SD) | | *d* | M (SD) | | *d* | M (SD) | | *d* |
| Besteiro et al. [24] | 6.8 (0.4) | 7.0 (0.3) | −0.57 | 6.3 (0.7) | 6.5 (0.4) | −0.35 | 5.4* (0.9) | 5.9 (0.7) | −0.62 | 85.3 (11.4) | 90.7 (7.3) | 0.56 | 18.9* (10.4) | 8.8 (8.1) | 1.08 | N/A | | |
| Burns et al. [29] Chervin et al. [30] | 8.0 (0.1) | 7.9 (0.1) | 0.09 | N/A | | | 7.0 (0.5) | 6.9 (0.5) | 0.20 | 87.5 (7.0) | 87.6 (5.9) | −0.01 | 50.0 (35.4) | 49.3 (27.6) | 0.02 | N/A | | |
| Côté & Moldofsky [67] | N/A | | | N/A | | | N/A | | | N/D | | | N/A | | | N/A | | |
| Drewes et al. [46] | 7.3 (0.2) | 7.2 (0.3) | 0.39 | 7.0 (0.2) | 6.9 (0.3) | 0.39 | 6.4 (0.4) | 6.7 (0.3) | −0.85 | 87.6* (5.5) | 92.3 (2.6) | −1.09 | 35.0* (23.4) | 17.1 (11.1) | 0.98 | N/A | | |
| Landis et al. [44] | 8.0 (1.0) | 7.9 (0.9) | 0.10 | 7.4 (1.2) | 7.4 (0.9) | 0.00 | 5.9 (1.1) | 6.2 (0.9) | −0.30 | 74.4* (12.1) | 78.3 (11.3) | −0.33 | N/A | | | 19.1 (9.5) | 16.7 (11.5) | 0.23 |
| Landis et al. [23] | N/A | | | N/A | | | 6.5 (1.0) | 6.5 (0.8) | 0.00 | 80.0* (10.0) | 85.0 (8.0) | −0.55 | N/A | | | 14.6 (8.7) | 11.1 (7.0) | 0.44 |
| Riva et al. [66] | 6.3* (0.9) | 6.9 (0.8) | −0.70 | 5.8* (1.1) | 6.6 (0.8) | −0.85 | 4.8 (1.2) | 5.8 (0.7) | −1.02 | 75.2* (13.1) | 85.7 (9.2) | −0.93 | N/A | | | N/A | | |
| Roehrs et al. [25] | N/A | | | N/A | | | 6.7* (0.1) | 7.2 (0.1) | −3.84 | N/A | | | 64.3* (8.1) | 40.2 (5.6) | 3.46 | N/A | | |
| Roizenblatt et al. [26] | N/A | | | N/A | | | N/A | | | N/D | | | N/A | | | N/A | | |
| Shaver et al. [27] | 7.9 (0.9) | 7.1 (1.0) | 0.84 | N/A | | | N/A | | | 88.0 (7.0) | 91.0 (5.0) | −0.49 | N/A | | | 11.6 (7.1) | 8.7 (4.9) | 0.47 |
| Statistical power | 0.33 (0.28) | | | 0.33 (0.34) | | | 0.48 (0.40) | | | 0.46 (0.33) | | | 0.67 (0.44) | | | 0.25 (0.17) | | |

| | SL N1 (min) | | | SL N2 (min) | | | Stage N1 (% TST) | | | Stage N2 (% TST) | | | Stage N3 (% TST) | | | Stage R (% TST) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | FMS | HC | ES | FMS | HC | ES | FMS | HC | ES | FMS | HC | ES | FMS | HC | ES | FMS | HC | ES |
| | M (SD) | | *d* | M (SD) | | *d* | M (SD) | | *d* | M (SD) | | *d* | M (SD) | | *d* | M (SD) | | *d* |
| Besteiro et al. [24] | 16.9 (16.8) | 26.5 (36.6) | −0.34 | N/A | | | 7.1 (4.5) | 11.8 (18.1) | −0.36 | 57.0* (9.4) | 48.5 (16.2) | 0.64 | 9.2[f]* (4.7) | 10.8 (4.5) | −0.36 | 16.5 (6.7) | 16.4 (5.2) | 0.02 |
| Burns et al. [29] Chervin et al. [30] | N/A | | | N/A | | | 6.4[b] (3.3) | 6.8 (3.9) | −0.11 | 51.6[b] (7.0) | 55.8 (6.6) | −0.62 | 19.0[b] (8.5) | 15.7 (7.3) | 0.42 | 22.9[b] (4.3) | 21.7 (5.0) | 0.26 |
| Côté & Moldofsky [67] | N/D | | | N/A | | | 4.9[c]* (2.6) | 1.8 (1.4) | 1.48 | N/A | | | N/A | | | N/A | | |
| Drewes et al. [46] | 22.7 (13.1) | 15.9 (10.4) | 0.57 | 6.6[d]* (4.7) | 3.0 (2.1) | 0.99 | 15.9[e]* (23.4) | 9.5 (5.7) | 0.37 | 198.0[e] (29.2) | 210.3 (18.0) | −0.51 | 34.6[e,f] (18.8) | 41.4 (16.8) | −0.38 | 106.3[e] (25.3) | 89.5 (18.3) | 0.76 |
| Landis et al. [44] | N/A | | | 27.4 (30.0) | 18.3 (13.3) | 0.39 | 11.5[c] (3.9) | 9.5 (3.9) | 0.51 | 40.0[c] (9.4) | 42.2 (10.4) | −0.22 | 10.4[c] (8.5) | 12.2 (5.8) | −0.25 | 19.1[c] (5.6) | 19.3 (6.6) | −0.03 |
| Landis et al. [23] | N/A | | | 23.4* (21.2) | 15.6 (12.7) | 0.45 | 12.7[c]* (4.8) | 10.5 (2.8) | 0.56 | 40.8[c]* (9.2) | 46.8 (7.7) | −0.70 | 12.9[c] (9.9) | 12.5 (7.6) | 0.04 | 18.5[c] (5.8) | 18.6 (6.4) | −0.02 |
| Riva et al. [66] | N/A | | | N/A | | | N/A | | | N/A | | | N/A | | | N/A | | |
| Roehrs et al. [25] | 14.4 (2.8) | 7.2 (1.3) | 3.30 | 23.7 (4.8) | 14.1 (3.3) | 2.33 | 8.6 (0.9) | 8.0 (0.8) | 0.70 | 60.3 (1.6) | 63.1 (2.2) | −1.45 | 9.4 (1.9) | 10.3 (1.9) | −0.47 | 21.6 (1.5) | 17.9 (1.6) | 2.38 |
| Roizenblatt et al. [26] | N/A | | | N/D | | | 13.0* (2.1) | 8.9 (2.4) | 1.82 | N/D | | | N/D | | | N/D | | |
| Shaver et al. [27] | N/A | | | 12.9 (11.6) | 12.4 (8.4) | 0.05 | 14.4[c]* (4.3) | 10.4 (3.7) | 1.00 | 46.7[c] (4.5) | 46.8 (11.0) | −0.01 | 3.7[c,f] (3.6) | 6.2 (6.6) | −0.47 | N/A | | |
| Statistical power | 0.50 (0.43) | | | 0.48 (0.37) | | | 0.49 (0.32) | | | 0.45 (0.36) | | | 0.18 (0.08) | | | 0.28 (0.38) | | |

| | SL REM (min) | | | Stage shifts (num) | | | Awakenings (num) | | | Arousals (num) | | | Fragmentation index | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | FMS | HC | ES | FMS | HC | ES | FMS | HC | ES | FMS | HC | ES | FMS | HC | ES |
| | M (SD) | | *d* | M (SD) | | *d* | M (SD) | | *d* | M (SD) | | *d* | M (SD) | | *d* |
| Besteiro et al. [24] | 129.5 (84.5) | 110.4 (61.1) | 0.26 | N/A | | | 70.3* (47.9) | 19.6 (13.1) | 1.44 | 17.0[a]* (13.2) | 8.7 (5.1) | 0.83 | N/A | | |
| Burns et al. [29] Chervin et al. [30] | N/A | | | 126.1* (27.5) | 107.0 (22.1) | 0.76 | N/A | | | 64.9 (39.4) | 43.3 (16.1) | 0.72 | N/A | | |
| Côté & Moldofsky [67] | N/A | | | N/A | | | N/D | | | N/A | | | N/A | | |
| Drewes et al. [46] | 84.4 (29.0) | 87.8 (23.2) | −0.13 | 89.4 (15.2) | 88.8 (15.0) | 0.04 | N/A | | | 51.9 (19.8) | 66.2 (28.8) | −0.58 | N/A | | |
| Landis et al. [44] | N/A | | | N/A | | | N/A | | | N/A | | | 8.2* (3.1) | 8.0 (3.1) | 0.06 |
| Landis et al. [23] | 72.8 (31.8) | 86.3 (41.4) | 0.45 | N/A | | | N/A | | | N/A | | | 8.6 (3.0) | 7.4 (2.2) | 0.46 |
| Riva et al. [66] | N/A | | | N/A | | | N/A | | | N/A | | | N/A | | |
| Roehrs et al. [25] | 99.2 (14.0) | 120 (15.9) | −1.39 | N/A | | | N/A | | | N/A | | | N/A | | |
| Roizenblatt et al. [26] | N/A | | | N/A | | | N/A | | | N/D | | | N/A | | |
| Shaver et al. [27] | N/A | | | 181.8 (64.5) | 143.1 (36.5) | 0.74 | N/A | | | N/D | | | 8.7 (3.5) | 7.0 (2.5) | 0.56 |
| Statistical power | 0.40 (0.41) | | | 0.32 (0.24) | | | 0.99 (N/A) | | | 0.52 (0.26) | | | 0.24 (0.23) | | |

*Note*. ES = Effect size; FMS = Fibromyalgia syndrome; HC = Healthy controls; M = Mean; N/A = Not measured; N/D = No differences; Num = Number; N1 = Stage 1 non-REM sleep; N2 = Stage 2 non-REM sleep; N3 = Stage 3 non-REM sleep; R = REM sleep; SD = Standard deviation; SL = Sleep latency; SPT = Sleep period time; TST = Total sleep time; WASO = Wake after sleep onset. A negative Cohen's *d* value represents that controls' results are higher.
*$p < .05$.
[a] Defined as K-complex followed by an explosion of alpha activity lasting less than five seconds.
[b] Percentages were referred to time in bed.
[c] Percentage was referred to sleep period time.
[d] Latency from sleep onset (N1).
[e] Numbers represent minutes.
[f] Mean and standard deviation computed from percentages of non-REM S3 and S4.

population. Since the clinical profiles of these patients are quite variable, FMS may not constitute a single clinical entity. Several authors have tried to construct FMS patient clusters according to their variations in symptoms and symptom severity [33,74]. Moreover, the relationships between sleep and FMS are quite complex, and it is well established that pain, psychological distress, and other somatic and psychological factors that have a key role in FMS can modify sleep patterns [12]. All of these cluster studies agree that sleep disturbances are key symptoms to differentiate patient subgroups. An open question is if objective disturbances might also have the potential to discriminate between FMS patients.

Of particular interest is the fact that the majority of studies failed to find disturbed α-EEG activity during sleep in FMS. α-EEG sleep was the first sleep disturbance proposed as an etiological factor in FMS [18], as it would be a marker of fragmented sleep similar to α-EEG activity appearing in healthy people in response to sleep depriving noise stimuli [75]. Moldofsky and colleagues, across their prolific research, proposed that α-EEG sleep in fronto-central derivations during NREM sleep might indicate a vigilant arousal state during sleep and a shift toward wakefulness in patients with FMS [19], suggesting that patients do not *disconnect* and rest appropriately resulting in complaints of unrefreshing sleep and subsequent pain. In recent years, however, this working hypothesis has been questioned (for a review, see [76]). Furthermore, the evidence from reviewed studies here indicates that α-EEG sleep should not be used to characterize sleep in FMS.

Regardless of the low-quality of most of the data and the great heterogeneity in both the study methodologies and outcomes, this systematic review shows that PSG alterations might validate sleep complaints in FMS. However, lighter and fragmented sleep, as described here in several FMS studies, is also present in other rheumatic conditions [77], psychopathological disorders [78], and even age-related changes [79]. It could therefore be the case that sleep architecture differs in severity among disorders, rather than qualitatively, with sleep-related disorders arrayed along a simple progression of increasing sleep disturbances [80]. Sleep architecture could be disturbed in a limited number of ways and it might not be possible to detail more than good or poor sleep quality. Although this explanation remains hypothetical, it is consistent with a recent theory that posits that poor sleep quality is a primary indicator of FMS onset rather than any specific type of sleep disturbance [17]. It is possible that this hypothesis results from the inability to find a valid explanatory theory for sleep disorders' physiology in FMS. Several authors have tried to identify the links between sleep physiology and chronic pain via the sleep-waking mechanisms and, in particular, the dopaminergic and norepinephrine systems, which are highly involved in arousal [81,82]. Additionally, considering all recent hypotheses about central sensitization in FMS [83], restorative functions of sleep on brain functions might have a significant role.

## *Concluding remarks*

Sleep disturbances characterize FMS regardless of the sleep assessment tool. Women with FMS complain of poor sleep, insufficient sleep, a large number of awakenings, and exhibit objective signs of less efficient, light and fragmented sleep. Clinical features and physiological abnormalities of sleep in FMS are important sources of information in the assessment and management of patients and in the pathophysiology of the syndrome. However, the role that sleep disturbances play in FMS is far from being settled. Current evidence could not confirm the importance of sleep physiology in the pathogenesis or maintenance of FMS symptoms.

**Table 11**
Comparison of microstructure parameters in patients with fibromyalgia syndrome vs. healthy controls.

| | Sleep parameters | FMS | HC | ES |
|---|---|---|---|---|
| | | M (SD) | | *d* |
| Besteiro et al. [24] | Epochs with 0–25% of alpha frequencies in N2, N3 | 1.56 (3.96) | 0.15 (0.67) | 0.496 |
| | Epochs with 26–50% of alpha frequencies in N2, N3 | 1.14 (3.45) | 0.05 (0.22) | 0.445 |
| | Epochs with 51–75% of alpha frequencies in N2, N3 | 0.60 (2.83) | 0.00 (0.00) | 0.299 |
| | Epochs with 76–100% of alpha frequencies in N2, N3 | 0.25 (1.41) | 0.00 (0.00) | 0.250 |
| Chervin et al. [30] | Alpha power during N3 ($\mu V^2$), M (SD) | 11.9 (1.09) | 11.5 (1.03) | 0.377 |
| | Alpha power during N3/alpha power during remaining sleep stages, M (SD) | 0.37 (0.32) | 0.25 (0.20) | 0.449 |
| Côté & Moldofsky [67] | Percentage of time with alpha frequency in N2, N3, N4[a] | *No differences* | | *N/A* |
| Drewes et al. [46] | Mean power in alpha band (% of total energy) during Non-REM sleep | 25.0 (8.6)*[b] | 21.6 (4.7) | 0.490 |
| | Mean power in alpha band (% of total energy) during Non-REM sleep in 1st cycle | 26.0 (9.9)*[b] | 21.7 (5.2) | 0.543 |
| | Mean power in alpha band (% of total energy) during Non-REM sleep in 2nd cycle | 22.9 (8.6)[b] | 20.8 (5.3) | 0.293 |
| Roizenblatt et al. [26] | Presence of phasic alpha sleep pattern, % of participants | 50 | 7 | *N/A* |
| | Presence of tonic alpha sleep pattern, % of participants | 20 | 9 | *N/A* |
| | Low presence of alpha activity, % of participants | 30* | 83.7 | *N/A* |
| Shaver et al. [27] | Ratio alpha/delta activity | *No differences* | | *N/A* |
| Landis et al. [23] 2004–2 | Sleep spindles in N2: number per minute, M (SD) | 3.8 (2.2)* | 5.4 (2.9) | −0.621 |
| | Sleep spindles in N2:duration (sec), M (SD) | 1.2 (0.2) | 1.1 (0.2) | 0.499 |
| | Sleep spindles in N2: spindle time per epoch (sec), M (SD) | 1.7 (1.2)* | 2.7 (1.8) | −0.653 |
| | Sleep spindles in N2: log normalized sigma power 12–12.5 Hz | Specific values not reported ↓* | Specific values not reported | *N/A* |
| | Sleep spindles in N2: log normalized sigma power 13–13.5 Hz | Specific values not reported ↓* | Specific values not reported | *N/A* |
| | Sleep spindles in N2: log normalized sigma power 14–14.5 Hz | Specific values not reported ↓* | Specific values not reported | *N/A* |

Note. ES = Effect size; FMS = Fibromyalgia syndrome; HC = Healthy controls; M = Mean; N/A = Not measured; SD = Standard deviation. A negative Cohen's *d* value represents that controls' results are higher.
*$p < .05$.
[a] For this variable, healthy control's sample size differed from original ($N = 7$).
[b] Mean and standard deviation computed from mean power in alpha-band during non-REM S2, and S3.

Please cite this article in press as: Diaz-Piedra C, et al., Sleep disturbances of adult women suffering from fibromyalgia: A systematic review of observational studies, Sleep Medicine Reviews (2014), http://dx.doi.org/10.1016/j.smrv.2014.09.001

Several theoretical approaches have tried, without success, to explain the relationship between sleep physiology and FMS symptoms. Further studies must be performed with higher methodological quality standards in order to elucidate whether sleep symptoms in patients with FMS reflect more than sleep misperception.

**Practice points**

1. Women with fibromyalgia syndrome exhibit more sleep complaints, including poorer sleep quality, fewer hours of sleep, greater nighttime awakenings, and non-restorative sleep.
2. Objective measures of sleep in this population are mixed and inconsistent, which might be related to underpowered studies. Even so, sleep in fibromyalgia syndrome seems to be less efficient, lighter and fragmented.
3. As part of the clinical work up, have pre-menopausal women with fibromyalgia syndrome maintain sleep diaries and rate their level of FMS pain/symptomatology to determine additional clinical interventions.
4. Despite mixed findings in the subjective and objective sleep literature and in view of the fact that a majority of women with fibromyalgia syndrome report sleep disturbances, provide sleep promotion techniques, including sleep hygiene, stimulus control and relaxation techniques.

**Research agenda**

Future research considerations:

1. Determine if disturbances in sleep physiology are intrinsic to the fibromyalgia syndrome and their role in the pathogenesis of its symptoms.
2. Assess norepinephrine levels during sleep hours to examine a relationship with hyperarousal status in fibromyalgia.
3. Examine if differences in patients' sleep physiology support the hypothesis of fibromyalgia heterogeneity.
4. Determine ways in which sleep disturbances influence daytime symptoms in fibromyalgia syndrome, including objective measures of sleepiness and arousal.
5. Analyze convergences/divergences between objective and subjective measures to validate sleep measures in chronic pain populations.
6. General methodological weaknesses have been found in most of the published studies. These recommendations will improve research designs in order to obtain consistent results:
   a. Enlarge the sample size until reaching the minimum number of participants required to ensure optimal statistical power (a minimum of 40 participants per group).
   b. Avoid the use of self-referred participants when possible, particularly if a comprehensive health check is not available.
   c. Achieve a representative sample through the selection of a random subset of patients and controls when excluding patients means a loss of statistical power and loss of generalizability.
   d. Control potential confounders – if it is not possible to obtain a random sample – by matching, stratifying or selecting appropriate samples, and/or using statistical control for confounding (including age, gender, ethnic group, educational level, marital status, body mass index, menopausal status, physical activity levels, health status, and medication intake).
   e. Comply with standards of recording techniques and current recommendations (following the American Academy of Sleep Medicine guidelines for standard polysomnography), including physiological status controls.
   f. Achieve more ecological validity by using home-setting polysomnographic recording and more reliability by assessing at least two nights.

## Declaration of interest

The authors report no conflicts of interest.

## Acknowledgments

CDP was supported by a FPU grant from the Spanish Ministry of Education (AP 2007-02965) and is currently supported by a UGR Postdoctoral Fellowship (2013 University of Granada Research Plan). LLDS is supported by the MEC-Fulbright Postdoctoral Fellowship program (grant PS-2010-0667) and the Talentia/Marie Curie Postdoctoral Fellowship program (grant Talentia Postdoc 267226). Research by GBC is funded by a Spanish Ministry of Economy and Competitiveness grant (State Secretariat for Research, Development and Innovation Secretary, EDU2010-21215). Research by AC is funded by a Spanish Ministry of Economy and Competitiveness grant (State Secretariat for Research, Development and Innovation Secretary, PSI2012-39292). We would like to thank M. I. Montañez and M. Garzón (Mind, Brain, and Behavior Research Center-CIMCYC; University of Granada; Spain) for their assistance during bibliographic research, and R. Fernandez-Mendez (Faculty of Medicine & Health Sciences; The University of Nottingham; UK) for her valuable advice. We also thank Pamela J. Osborn Popp (New York University; USA) for her helpful comments on earlier versions of the text and language revisions.

## References

[1] Wolfe F, Smythe HA, Yunus MB, Bennett RM, Bombardier C, Goldenberg DL, et al. The American College of Rheumatology 1990 criteria for the classification of fibromyalgia. Arthritis Rheum 1990;33:160–72.
[2] Wolfe F, Clauw DJ, Fitzcharles M-A, Goldenberg DL, Häuser W, Katz RS, et al. Fibromyalgia criteria and severity scales for clinical and epidemiological studies: a modification of the ACR preliminary diagnostic criteria for fibromyalgia. J Rheumatol 2011;38:1113–22.
[3] Branco JC, Bannwarth B, Failde I, Abello Carbonell J, Blotman F, Spaeth M, et al. Prevalence of fibromyalgia: a survey in five European countries. Semin Arthritis Rheum 2010;39:448–53.
[4] Lachaine J, Beauchemin C, Landry P-A. Clinical and economic characteristics of patients with fibromyalgia syndrome. Clin J Pain 2010;26:284–90.
*[5] Wagner J-S, Chandran A, DiBonaventura M, Cappelleri JC. The costs associated with sleep symptoms among patients with fibromyalgia. Expert Rev Pharmacoecon Outcomes Res 2013;13:131–9.
[6] Birtane M, Uzunca K, Taştekin N, Tuna H. The evaluation of quality of life in fibromyalgia syndrome: a comparison with rheumatoid arthritis by using SF-36 Health Survey. Clin Rheumatol 2007;26:679–84.
[7] Rutledge DN, Mouttapa M, Wood PB. Symptom clusters in fibromyalgia: potential utility in patient assessment and treatment evaluation. Nurs Res 2009;58:359–67.

* The most important references are denoted by an asterisk.

[8] Rutledge DN, Jones K, Jones CJ. Predicting high physical function in people with fibromyalgia. J Nurs Scholarsh 2007;39:319–24.
*[9] Smith MT, Haythornthwaite JA. How do sleep disturbance and chronic pain inter-relate? Insights from the longitudinal and cognitive-behavioral clinical trials literature. Sleep Med Rev 2004;8:119–32.
[10] Affleck G, Urrows S, Tennen H, Abeles M. Sequential daily relations of sleep, pain intensity, and attention to pain among women with fibromyalgia. Pain 1996;68:363–8.
[11] Finan PH, Goodin BR, Smith MT. The association of sleep and pain: an update and a path forward. J Pain 2013;14:1539–52.
[12] Nicassio PM, Moxham EG, Schuman CE, Gevirtz RN. The contribution of pain, reported sleep quality, and depressive symptoms to fatigue in fibromyalgia. Pain 2002;100:271–9.
[13] Korszun A, Young EA, Engleberg NC, Brucksch CB, Greden JF, Crofford LA. Use of actigraphy for monitoring sleep and activity levels in patients with fibromyalgia and depression. J Psychosom Res 2002;52:439–43.
[14] Edinger JD, Wohlgemuth WK, Krystal AD, Rice JR. Behavioral insomnia therapy for fibromyalgia patients: a randomized clinical trial. Arch Intern Med 2005;165:2527–35.
[15] Martínez MP, Miró E, Sánchez AI, Díaz-Piedra C, Cáliz R, Vlaeyen JWS, et al. Cognitive-behavioral therapy for insomnia and sleep hygiene in fibromyalgia: a randomized controlled trial. J Behav Med 2014;37:683–97.
[16] Bennett RM. Beyond fibromyalgia: ideas on etiology and treatment. J Rheumatol 1989;19:185–91.
*[17] Hamilton NA, Atchley RA, Karlson CW, Taylor D, McCurdy D. The role of sleep and attention in the etiology and maintenance of fibromyalgia. Cogn Ther Res 2012;36:81–93.
[18] Moldofsky H, Scarisbrick P, England R, Smythe H. Musculosketal symptoms and non-REM sleep disturbance in patients with “fibrositis syndrome” and healthy subjects. Psychosom Med 1975;37:341–51.
*[19] Moldofsky H. The significance of the sleeping–waking brain for the understanding of widespread musculoskeletal pain and fatigue in fibromyalgia syndrome and allied syndromes. Jt Bone Spine 2008;75:397–402.
[20] Hamilton NA, Affleck G, Tennen H, Karlson C, Luxton D, Preacher KJ, et al. Fibromyalgia: the role of sleep in affect and in negative event reactivity. Health Psychol 2008;27:490–7.
[21] Drewes AM, Svendsen L, Nielsen KD, Taagholt SJ, Bjerregård K. Quantification of alpha-EEG activity during sleep in fibromyalgia: a study based on ambulatory sleep monitoring. J Musculoskelet Pain 1994;2:33–53.
[22] Landis CA, Lentz MJ, Rothermel J, Riffle SC, Chapman D, Buchwald D, et al. Decreased nocturnal levels of prolactin and growth hormone in women with fibromyalgia. J Clin Endocrinol Metab 2001;86:1672–8.
[23] Landis CA, Lentz MJ, Tsuji J, Buchwald D, Shaver JLF. Pain, psychological variables, sleep quality, and natural killer cell activity in midlife women with and without fibromyalgia. Brain Behav Immun 2004;18:304–13.
[24] Besteiro JL, Suárez TV, Arboleya L, Muñiz J, Lemos S, Álvarez A. Sleep architecture in patients with fibromyalgia. Psicothema 2011;23:368–73.
[25] Roehrs T, Diederichs C, Gillis M, Burger AJ, Stout RA, Lumley MA, et al. Nocturnal sleep, daytime sleepiness and fatigue in fibromyalgia patients compared to rheumatoid arthritis patients and healthy controls: a preliminary study. Sleep Med 2013;14:109–15.
[26] Roizenblatt S, Moldofsky H, Benedito-Silva AA, Tufik S. Alpha sleep characteristics in fibromyalgia. Arthritis Rheum 2001;44:222–30.
[27] Shaver JLF, Lentz M, Landis CA, Heitkemper MM, Buchwald DS, Woods NF. Sleep, psychological distress, and stress arousal in women with fibromyalgia. Res Nurs Health 1997;20:247–57.
[28] Drewes AM, Nielsen KD, Taagholt SJ, Bjerregård K, Svendsen L, Gade J. Sleep intensity in fibromyalgia: focus on the microstructure of the sleep process. Br J Rheumatol 1995;34:629–35.
[29] Burns JW, Crofford LJ, Chervin RD. Sleep stage dynamics in fibromyalgia patients and controls. Sleep Med 2008;9:689–96.
[30] Chervin RD, Teodorescu M, Kushwaha R, Deline AM, Brucksch CB, Ribbens-Grimm C, et al. Objective measures of disordered sleep in fibromyalgia. J Rheumatol 2009;36:2009–16.
[31] Rains J, Penzien D. Sleep and chronic pain challenges to the α-EEG sleep pattern as a pain specific sleep anomaly. J Psychosom Res 2004;56:255–6.
[32] Okifuji A, Hare BD. Nightly analyses of subjective and objective (actigraphy) measures of sleep in fibromyalgia syndrome: what accounts for the discrepancy? Clin J Pain 2011;27:289–96.
[33] Rehm SE, Koroschetz J, Gockel U, Brosz M, Freynhagen R, Tölle TR, et al. A cross-sectional survey of 3035 patients with fibromyalgia: subgroups of patients with typical comorbidities and sensory symptom profiles. Rheumatology 2010;49:1146–52.
*[34] Abad VC, Sarinas PSA, Guilleminault C. Sleep and rheumatologic disorders. Sleep Med Rev 2008;12:211–28.
[35] Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JPA, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. PLoS Med 2009;6:e1000100.
[36] Deeks JJ, Dinnes J, D'Amico R, Sowden AJ, Sakarovitch C, Song F, et al. Evaluating non-randomised intervention studies. Health Technol Assess 2003;7:1–179.
[37] Roizenblatt S, Benedito-Silva AA, Tufik S, Moldofsky H. Características do sono alfa na fibromialgia. Rev Bras Reum 2002;42:15–24.
[38] Martinez JE, Ferraz MB, Sato EI, Atra E. Avaliaçao seqüencial do impacto fibromialgia e artrite reumatóide na qualidade de vida. Rev Bras Reum 1994;34:309–16.
[39] Martinez JE, Ferraz MB, Sato EI, Atra E. Fibromyalgia versus rheumatoid arthritis: a longitudinal comparison of the quality of life. J Rheumatol 1995;22:270–4.
[40] Parrish BP, Zautra AJ, Davis MC. The role of positive and negative interpersonal events on daily fatigue in women with fibromyalgia, rheumatoid arthritis, and osteoarthritis. Health Psychol 2008;27:694–702.
[41] Zautra AJ, Fasman R, Parish BP, Davis MC. Daily fatigue in women with osteoarthritis, rheumatoid arthritis, and fibromyalgia. Pain 2007;128:128–35.
[42] Shaver JLF, Wilbur J, Robinson FP, Wang E, Buntin MS. Women's health issues with fibromyalgia syndrome. J Womens Health 2006;15:1035–45.
[43] Borman P, Çeliker R. A comparative analysis of quality of life in rheumatoid arthritis and fibromyalgia. J Musculoskelet Pain 1999;7:5–14.
[44] Landis CA, Lentz MJ, Rothermel J, Buchwald D, Shaver JLF. Decreased sleep spindles and spindle activity in midlife women with fibromyalgia and pain. Sleep 2004;27:741–50.
[45] Bagge E, Bengtsson BA, Carlsson L, Carlsson J. Low growth hormone secretion in patients with fibromyalgia – a preliminary report on 10 patients and 10 controls. J Rheumatol 1998;25:145–8.
[46] Drewes AM, Gade J, Nielsen KD, Bjerregård K, Taagholt SJ, Svendsen L. Clustering of sleep electroencephalographic patterns in patients with the fibromyalgia syndrome. Br J Rheumatol 1995;34:1151–6.
[47] Malin K, Littlejohn GO. Neuroticism in young women with fibromyalgia links to key clinical features. Pain Res Treat 2012;2012. ID730741.
[48] Akkaya N, Akkaya S, Atalay NS, Acar M, Catalbas N, Sahin F. Assessment of the relationship between postural stability and sleep quality in patients with fibromyalgia. Clin Rheumatol 2013;32:325–31.
[49] Lerma C, Martinez A, Ruiz N, Vargas A, Infante O, Martinez-Lavin M. Nocturnal heart rate variability parameters as potential fibromyalgia biomarker: correlation with symptoms severity. Arthritis Res Ther 2011;13:R185.
[50] Munguía-Izquierdo D, Legaz-Arrese A. Determinants of sleep quality in middle-aged women with fibromyalgia syndrome. J Sleep Res 2012;21:73–9.
[51] Tander B, Atmaca A, Aliyazicioglu Y, Canturk F. Serum ghrelin levels but not GH, IGF-1 and IGFBP-3 levels are altered in patients with fibromyalgia syndrome. Jt Bone Spine 2007;74:477–81.
[52] Tüzün EH, Albayrak G, Eker L, Sözay S, Daşkapan A. A comparison study of quality of life in women with fibromyalgia and myofascial pain syndrome. Disabil Rehabil 2004;26:198–202.
[53] Ulus Y, Akyol Y, Tander B, Durmus D, Bilgici A, Kuru O. Sleep quality in fibromyalgia and rheumatoid arthritis: associations with pain, fatigue, depression, and disease activity. Clin Exp Rheumatol 2011;29:92–6.
[54] Homann D, Louzada F m, Góes S m, Roizenblatt S, Lopes A l, de Oliveira Á r, et al. Acylated ghrelin: a potential marker for fibromyalgia? Eur J Pain 2013;17:1216–24.
[55] Olama SM, Elsaid TO, El-Arman M. Serum Leptin in Egyptian patients with fibromyalgia syndrome: relation to disease severity. Int J Rheum Dis 2013;16:583–9.
[56] Akdoğan S, Ayhan FF, Yıldırım S, Borman P. Impact of fatigue on cognitive functioning among premenopausal women with fibromyalgia syndrome and rheumatoid arthritis: the controlled study. J Musculoskelet Pain 2013;21:135–46.
[57] Can SS, Can AG. Validity and reliability of the clock drawing test as a screening tool for cognitive impairment in patients with fibromyalgia. Compr Psychiatry 2012;53:81–6.
[58] Dick BD, Verrier MJ, Harker KT, Rashiq S. Disruption of cognitive function in fibromyalgia syndrome. Pain 2008;139:610–9.
[59] Gur A, Karakoc M, Erdogan S, Nas K, Cevik R, Sarac AJ. Regional cerebral blood flow and cytokines in young females with fibromyalgia. Clin Exp Rheumatol 2002;20:753–60.
[60] Miró E, Martínez MP, Sánchez AI, Prados G, Medina A. When is pain related to emotional distress and daily functioning in fibromyalgia syndrome? The mediating roles of self-efficacy and sleep quality. Br J Health Psychol 2011;16:799–814.
[61] Miró E, Martínez MP, Sánchez AI, Prados G, Diener FN. Papel de las cogniciones disfuncionales sobre el sueño en la baja calidad del sueño informada por los pacientes con fibromialgia [The role of dysfunctional beliefs in the reported poor sleep quality in patients with fibromyalgia]. Psicol Conduct 2012;20:699–718.
[62] Buysse DJ, Reynolds III CF, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh sleep quality index: a new instrument for psychiatric practice and research. Psychiatry Res 1989;28:193–213.
[63] Carpenter JS, Andrykowski MA. Psychometric evaluation of the Pittsburgh Sleep Quality Index. J Psychosom Res 1998;45:5–13.
[64] Landis CA, Frey CA, Lentz MJ, Rothermel J, Buchwald D, Shaver JLF. Self-reported sleep quality and fatigue correlates with actigraphy in midlife women with fibromyalgia. Nurs Res 2003;52:140–7.
[65] Rechtschaffen A, Kales A. A manual of standardized terminology, techniques and scoring system for sleep stages of human subjects. UCLA. Los Angeles: US Government Printing Office, US Public Health Service; 1968.
[66] Riva R, Mork PJ, Westgaard RH, Rø M, Lundberg U. Fibromyalgia syndrome is associated with hypocortisolism. Int J Behav Med 2010;17:223–33.
[67] Côté KA, Moldofsky H. Sleep, daytime symptoms, and cognitive performance in patients with fibromyalgia. J Rheumatol 1997;24:2014–23.

Please cite this article in press as: Diaz-Piedra C, et al., Sleep disturbances of adult women suffering from fibromyalgia: A systematic review of observational studies, Sleep Medicine Reviews (2014), http://dx.doi.org/10.1016/j.smrv.2014.09.001

[68] Cohen J. Statistical power analysis for the behavioral sciences. L. Erlbaum Associates; 1988.
[69] Nir Y, Staba RJ, Andrillon T, Vyazovskiy VV, Cirelli C, Fried I, et al. Regional slow waves and spindles in human sleep. Neuron 2011;70:153–69.
[70] Fernandez-Mendoza J, Vgontzas AN, Bixler EO, Singareddy R, Shaffer ML, Calhoun SL, et al. Clinical and polysomnographic predictors of the natural history of poor sleep in the general population. Sleep 2012;35:689–97.
[71] Grandner MA, Petrov ME, Rattanaumpawan P, Jackson N, Platt A, Patel NP. Sleep symptoms, race/ethnicity, and socioeconomic position. J Clin Sleep Med 2013;9:897–905.
[72] Sameni R, Shamsollahi MB, Senhadji L. Processing polysomnographic signals using independent component analysis. In: Proc Int. Conf. Biomed. Eng., Innsbruck, Autriche; 2004. p. 193–6.
[73] Iber C, Ancoli-Israel S, Chesson A, Quan SF, for the American Academy of Sleep Medicine. The AASM manual for the scoring of sleep and associated events: rules, terminology and technical specifications. 1st ed. Westchester, Illinois: American Academy of Sleep Medicine; 2007.
[74] Calandre EP, Garcia-Carrillo J, Garcia-Leiva JM, Rico-Villademoros F, Molina-Barea R, Rodriguez-Lopez CM. Subgrouping patients with fibromyalgia according to the results of the fibromyalgia impact questionnaire: a replication study. Rheumatol Int 2011;31:1555–9.
[75] Moldofsky H, Scarisbrick P. Induction of neurasthenic musculoskeletal pain syndrome by selective sleep stage deprivation. Psychosom Med 1976;38:35–44.
*[76] Mahowald ML, Mahowald MW. Nighttime sleep and daytime functioning (sleepiness and fatigue) in less well-defined chronic rheumatic diseases with particular reference to the “alpha-delta NREM sleep anomaly”. Sleep Med 2000;1:195–207.
[77] Taylor-Gjevre RM, Gjevre JA, Nair B, Skomro R, Lim HJ. Components of sleep quality and sleep fragmentation in rheumatoid arthritis and osteoarthritis. Musculoskelet Care 2011;9:152–9.
[78] Riemann D. Insomnia and comorbid psychiatric disorders. Sleep Med 2007;8(Suppl. 4):S15–20.
[79] Ohayon MM, Carskadon MA, Guilleminault C, Vitiello MV. Meta-analysis of quantitative sleep parameters from childhood to old age in healthy individuals: developing normative sleep values across the human lifespan. Sleep 2004;27:1255–73.
[80] Hudson JI, Pope HG, Sullivan LE, Waternaux CM, Keck PE, Broughton RJ. Good sleep, bad sleep: a meta-analysis of polysomnographic measures in insomnia, depression, and narcolepsy. Biol Psychiatry 1992;32:958–75.
[81] Monti JM, Monti D. The involvement of dopamine in the modulation of sleep and waking. Sleep Med Rev 2007;11:113–33.
*[82] Finan PH, Smith MT. The comorbidity of insomnia, chronic pain, and depression: dopamine as a putative mechanism. Sleep Med Rev 2013;17:173–83.
[83] Meeus M, Nijs J. Central sensitization: a biopsychosocial explanation for chronic widespread pain in patients with fibromyalgia and chronic fatigue syndrome. Clin Rheumatol 2007;26:465–73.
[84] Kashikar-Zuck S, Ting TV. Juvenile fibromyalgia: current status of research and future developments. Nat Rev Rheumatol 2014;10:89–96.
[85] Mogil JS, Bailey AL. Sex and gender differences in pain and analgesia. Prog Brain Res 2010;186:141–57.
*[86] Krystal AD, Edinger JD. Measuring sleep quality. Sleep Med 2008;9(Suppl. 1):S10–7.
[87] Lario BA, Valdivielso JLA, López JA, Soteres CM, Bañuelos JLV, Cabello AM. Fibromyalgia syndrome: overnight falls in arterial oxygen saturation. Am J Med 1996;101:54–60.
[88] Lario BA, Valdivielso JLA, López JA, Soteres CM, Bañuelos JLV, Cabello AM. Síndrome de fibromialgia: características clínicas de las pacientes españolas [Fibromyalgia syndrome: clinical features of Spanish patients]. Rev Esp Reumatol 1996;23:76–82.
[89] Martinez JE, Barauna Filho IS, Kubokawa K, Pedreira IS, Machado LAM, et al. Comparação clínica e funcional de pacientes com fibromialgia e dor miofascial. Acta Fisiátrica 1998;5:159–63.
[90] Oncü J, Başoğlu F, Kuran B. A comparison of impact of fatigue on cognitive, physical, and psychosocial status in patients with fibromyalgia and rheumatoid arthritis. Rheumatol Int 2013;33:3031–7.
[91] Osorio CD, Gallinaro AL, Lorenzi-Filho G, Lage LV. Sleep quality in patients with fibromyalgia using the Pittsburgh Sleep Quality Index. J Rheumatol 2006;33:1863–5.

Please cite this article in press as: Diaz-Piedra C, et al., Sleep disturbances of adult women suffering from fibromyalgia: A systematic review of observational studies, Sleep Medicine Reviews (2014), http://dx.doi.org/10.1016/j.smrv.2014.09.001